THE SYSTEMIC INFLAMMATORY RESPONSE TO DENTAL PLAQUE

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ABSTRACT

Vivian Y. Wahaidi

The Systemic Inflammatory Response to Dental Plaque

Introduction: Bacteremia involving oral bacteria and the systemic inflammatory responses are mechanisms that could causally link oral and systemic diseases. Objective: To use an experimental gingivitis model (EGM) in 2 clinical studies to 1) examine the systemic inflammatory responses to dental plaque, and assess racial differences in these responses; 2) determine whether dental plaque accumulation causes bacteremia and subsequent systemic responses following toothbrushing. Additionally, a laboratory study was conducted to examine the interaction between circulating human neutrophils and *Fusobacterium nucleatum*. Methods: For both clinical studies, healthy adults, aged 18-31 years, were recruited. In the first study, black and white, males and females participated in a 21-day EGM; in the second study, white adults participated in a 7-day EGM. In both studies, subjects visited the clinic weekly for: 1) measurement of the plaque index (PI) and gingival index (GI); 2) collection of peripheral blood samples to evaluate systemic markers of inflammation. In the second study, to analyze bacteremic episodes during the experimental phase, peripheral blood samples were collected at baseline and at 0.5, 5, and 30 minutes post-toothbrushing. In the laboratory study, interactions between *F. nucleatum* and circulating neutrophils were examined using a luminol-enhanced chemiluminescence assay. Results: During the experimental phases of both clinical studies, PI and GI increased ($p<0.05$) with a correlation between PI and GI ≥ 0.79. In the first study, dental plaque accumulation resulted in a systemic response that manifested as

changes ($p<0.05$) in the level of inflammatory markers, hematologic factors, markers of lipid metabolism, and markers of metabolic change. This systemic response differed between individuals of different gender and race. In the second study, bacteremic episodes and changes in hematologic factors were observed post-toothbrushing during the experimental phase. Activation of neutrophils with *F. nucleatum*, in the laboratory study, increased the levels of neutrophil chemiluminescence ($p<0.05$). Conclusions: Overall, the findings of these investigations may shed light on the mechanistic pathways by which oral infection may impose risk for systemic diseases and provide some evidence to support a possible causal association between oral and systemic diseases. The clinical significance of this in systemic inflammatory diseases requires further investigation.

Michael J. Kowolik, B.D.S., Ph.D., Chair

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LIST OF ABBREVIATIONS

AHA	American Heart Association
ANOVA	Analysis of Variance
ATCC	American Tissue Culture Collection
BMI	Body Mass Index
CHD	Coronary Heart Disease
CO	Carbon Monoxide
CRP	C Reactive Protein
ESR	Erythrocyte Sedimentation Rate
fMLP	formyl-methionyl-leucyl-phenylalanine
GCRC	General Clinical Research Center
GI	Gingival Index
Hb	Hemoglobin
Hct	Hematocrit
HDL	High Density Lipoprotein
IL	Interleukin
IRB	Institutional Review Board
LDL	Low Density Lipoprotein
MCH	Mean Corpuscular Hemoglobin
MCHC	Mean Corpuscular Hemoglobin Concentration
MCV	Mean Corpuscular Volume
MPV	Mean Platelet Volume
OH	Oral Hygiene

OHI	Oral Hygiene Instructions
OHRI	Oral Health Research Institute
PBS	Phosphate Buffered Saline
PCR	Polymerase Chain Reaction
PI	Plaque Index
r	Correlation Coefficient
RBC	Red Blood Cell
RPMI	Roswell Park Memorial Institute
SD	Standard Deviation
SE	Standard Error
TNF	Tumor Necrosis Factor
UV	Ultra Violet
WBC	White Blood Cell

LIST OF APPENDICES